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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,140	01/22/2004	Hing C. Wong	TNA-005.05	6085

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,140	WONG ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed 4 December 2006 is acknowledged. Claim 37, 44 and 50 are amended. Claims 43 and 45-46 are withdrawn. Claims 37-42, 44 and 47-55 are under consideration.

Objections/Rejections withdrawn

Claim Objections

The objection to claim 44 for depending from withdrawn claim 43 is withdrawn in response to Applicants' amendment of the claims.

Information Disclosure Statement

The issues raised by the Examiner in the Office action mailed 16 May 2006 regarding the information disclosure statement filed 10/3/2005 and 1/23/2006 for failure to comply with 37 CFR 1.98(a)(2) and 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance of Japanese Patent no: 1-503438 is withdrawn in response to Applicants' submission of an information disclosure sheet on 7 November 2006.

Claim Rejections - 35 USC § 112, second paragraph

The rejection of claim 37 under 35 U.S.C. 112, second paragraph, as being indefinite for insufficient antecedent basis for "the complex" is withdrawn in response to amendment.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claim 44 under 35 U.S.C. 112, first paragraph is withdrawn in response to Applicants' amendment of the claims.

Double Patenting

Upon further consideration the provisional rejection of claims 37 and 40 on the ground of nonstatutory double patenting over claims 21, 23, 24, 29 and 30 of copending Application No. 11/311,702 is withdrawn.

Objections/Rejections Maintained

Priority

The issue raised by the Examiner in the Office action mailed 16 May 2006 regarding Applicants' non-compliance with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as because the disclosure of the

prior-filed application, Application No. 10/293,417, (and its parent applications, now U.S. Patents 6,555,319 and 5,986,065) fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application, because the '417 application does not provide enablement or written description for ***treatment of sepsis*** with the claimed antibodies, thus the effective filing date for the application is 22 January 2004 is maintained. The '417 application contains "septic shock syndrome" at paragraph [0073] in the following context:

> [0073] As also discussed above, antibodies of the invention can be employed to detect native human TF in a biological sample, particularly native TF associated with a blood clot. Exemplary biological samples include blood plasma, serum, saliva, urine, stool, vaginal secretions, bile, lymph, ocular humors, cerebrospinal fluid, cell culture media, and tissue, particularly vascular tissues such as cardiac tissue. Samples may be suitably obtained from a mammal suffering from or suspected of suffering from a thrombosis, preferably restenosis, associated with, e.g., an invasive medical procedure such as cardiopulmonary bypass surgery; a heart ailment such as myocardial infarction, cardiomyopathy, valvular heart disease, unstable angina, or artrial fibrillation associated with embolization; a coagulopathy including disseminated intravascular coagulation, deployment of an implementation such as a stent or catheter; shock (e.g., septic shock syndrome), vascular trauma, liver disease, heat stroke, malignancies (e.g., pancreatic, ovarian, or small lung cell carcinoma), lupus, eclampsia, perivascular occlusive disease, and renal disease.

Applicants point out at p. 6, 1st paragraph of their arguments that treatment of septic shock is supported in the instantly claimed method at column 12, lines 34-35 of U.S. Patent 5,986,065. The same passage cited above can be found in the '065 patent, in other words, while the earlier applications disclose diagnosis of septic shock syndrome with the rcited antibodies, it does not disclose treatment either ipsis verbis or by natural flow from the specification. Finally, an evaluation of working examples in the

prior filed applications are not commensurate in scope with treatment of septic shock syndrome. Absent persuasive evidence to the contrary, the prior filed applications cannot provide enablement or written description for the instantly claimed methods, and the effective filing date for the instantly claimed method is 22 January 2004.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 37-42, 47-55 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating septic shock syndrome in a mammal comprising administering to the mammal the antibody having a sequence represented by SEQ ID NO: 4, does not reasonably provide enablement for preventing septic shock syndrome or treatment with other antibodies is withdrawn in part in response to Applicants' amendment of the claims to omit reference to "prevention". However, the rejection of claims 37-42, 44, 47-55 is maintained with respect to the specification not being enabled for treatment of sepsis with antibodies other than SEQ ID NO: 4.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" were mentioned in the previous Office action mailed 16 May 2006. These factors include, but are not

limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Applicants' state at p. 5, 2nd paragraph that claim 15 of U.S. Patent 6,555,319 recites, "[an] antibody that binds native human tissue factor to form a complex whereby factor X binding to the complex is inhibited," and that providing further written description and enablement for antibodies that bind human tissue factor to form a complex whereby factor X binding to the complex is inhibited, the instant specification also describe in example 9 a septic shock model in rhesus monkeys.

This argument has been fully considered but is not found persuasive. The allowed claim of the '319 patent is to an antibody, not a therapeutic method, thus the standard is different for methods of treatment. There is no structural definition of the antibody in claim 37, but rather functional limitation in terms of a negative recitation Treatment is not defined in the specification, but is a well known term in the art defined as care by procedures or applications that are intended to relieve illness or injury. Undue experimentation would be required to determine all of the antibodies encompassed by claim 37 that would be useful in the relief of septic shock syndrome. The working example (example 9) demonstrates that infusion with the antibody led to a greatly increased average survival time, 111 hours vs. 16 hours with saline (since there was only an n=2, no statistical significance can be attributed to the finding).

Nevertheless, though the results are promising, the data are not commensurate in scope with the claim which encompasses any antibody (no structural limitation) any antibody that binds to any epitope of native human tissue factor. The phrase in claim 37, "whereby factor X binding to the complex is inhibited and factor VII or VIIa binding to tissue factor is not inhibited" is a negative recitation of function and does not effectively limit the claimed invention in a method claim. Again, unlike the previously allowed claim 15 of the '319 patent, which was to a product, the instant claims are to therapeutic methods, which have different considerations under enablement because the skilled artisan must perform undue experimentation to determine which antibodies having the recited negative recitation of function (in the absence of a structural limitation) could be used to treat septic shock syndrome. The previous Office action contained the Examiner's explanation of why antibody therapeutics in general is less predictable than antibody production (see Office action mailed 16 May 2006, p. 7-8).

In summary, due to the large quantity of experimentation necessary to determine the epitopes on native tissue factor where the recited antibody must bind and to establish a protocol for the treatment of septic shock, the lack of direction/guidance presented in the specification regarding and the absence of working examples directed to the same, the complex nature of the invention (antibody therapeutics), the unpredictability of antibody therapy and prevention in the prior art (please refer to p. 7-8 of previous Office action mailed 16 May 2006), and the breadth of the claims which fail to recite negative functional limitations in the absence of structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed

invention in its full scope, and the rejection under 35 U.S.C. 112, first paragraph for scope of enablement is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 37-42, 44, 47-55 under 35 U.S.C. 103(a) as being obvious over Wong et al. (WO 98/40408, published 17 September 1998) in view of Taylor (Crit Care Med. 2001, 29(7 Suppl): S78-89) is maintained for reasons of record and the following.

Applicants argue at p. 6, 1st full paragraph, that the Wong et al. is not available as prior art because it was published after 10 March 1997, to which the instant application claims benefit.

This argument has been fully considered but is not found persuasive, because as noted in the section under Priority, unless the Applicants can perfect the claim to benefit under 35 U.S.C. 119 (e), because the prior applications did not set forth that treatment was considered part of the invention, the effective filing date has been determined to be 22 January 2004.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

A representative number of provisional obviousness type-double patenting rejections were made in the Office action mailed 16 May 2006. It is noted that Applicants' have agreed to file a terminal disclaimer with respect to those copending patent applications upon the indication of allowable subject matter. In the interim the rejections remain of record.

The provisional rejection of claims 37, 38, 40, 41, 42, 47, 48, 49, 50 and 51 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32, 34, 35, 38, 46, 47 and 48 of copending Application No. 10/310,113 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claims 37, 38, 39, 40, 41, 42, 44, 47, 50 51, 52, 53 and 54 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37, 38, 39, 40, 41, 42, 43, 44, 45, 48, 53, 54, 55 and 57 of copending Application No. 10/618,338 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claim 37 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25, 26, 27 and 33 of copending Application No. 11/087,528 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claims 37, 47, 49, 50 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 66 of copending Application No. 11/122,622 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claims 37, 38, 39, 40, 42, 47, 50 and 51 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 10-12 of copending Application No. 11/311,702 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D. can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

Christina Borgeest, Ph.D.

ELIZABETH KEMMERER
PRIMARY EXAMINER